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21 August, 1951.

Dear Luca,

I would like to congratulate you on your paper, the subject matter of which, & the discussion, I thought excellent. You have obviously done much more work than I have. I don't know whether this is due to your greater innate energy or to your having technical assistance! Reading your paper made me realize the deficiencies in my own & led me to think that perhaps I have been rather unwise to attempt its theories at this early stage. Actually I have now cut out all my *phage* analogies which (Vollmer tells me) are unsound. As regards your paper, I thought most of the editorial & referee's criticisms fair & valid. I think that it would have been impossible for the general reader to read & understand without a great deal of effort. I have now finished revising it & think I have done it with some success. All I have actually done is to classify parts of it under headings where I thought others helped, altered the construction of a considerable number of long sentences, added a few explanations where I thought the technological description was too difficult for the uninitiated reader & changed a few rather "unenglish" phrases. I hope you will not mind my taking these liberties with your paper but in fact I think you will find it in no way radically altered. I have typed it with triple spacing so that you can re-alter it as you wish. I will send it to the editor for approval & will bring it to Italy with me, together with the annotated original. It is hardly worth sending it by post at this stage. You need not thank me. I enjoyed doing

it because it made me read & absorb your views much more closely & deeply than I would otherwise have done. About Table 2. The trouble here is that the reader has to remember what A means & B means, in addition to 1, 2, 3, 4, 5, 6, (in terms of L, G, M, X, F markers) before he can start to appreciate the significance of the actual data. It would help a lot if the six columns could be headed with particulars of the actual work, thus:

No. of prototrophs showing various arrangements of
Lac, Gal, Mal, Xyl, Ara markers from crosses:

Patterns of L,G,M,X,F markers characters	No. of prototrophs showing various arrangements of Lac, Gal, Mal, Xyl, Ara markers from crosses:					
	1.	2.	3.	4.	5.	
L G M X F x A						15-6
- - - - -	1			14		
- - - - +	290		25			
+ + - - +	208	246		1		2
- + + + -						

Key at bottom, thus - to L = Lactose.

G = Galactose.

X = Xylose &c.

+ = sugar fermented.

- = absence of fermentation.

And is there any need to have the LGMXA patterns arranged to read ~~up~~ head-to-tail for columns 4, 5, 6? It seems to me much simpler to read right across all seven columns. This makes comparison easy without affecting any of the information presented. You may have some special point to make by the "head-to-tail" system, but I don't see it.

I feel that the major criticism which can be made against my own work - & a very valid one - is that it has been mainly concerned with only two strains. But unless one is in the fortunate position of being able to hand out various aspects of the problem to students, as Dr. Gustav Leichtburg does (not to speak of his wife!), it is a nice point whether to make as much progress as possible with one system or to consolidate your position in depth as you go along, which may prove tedious & slow. I have done only one significant

(2)

experiment recently but it may interest you to hear of it now as I propose to mention it at Palaya. I reasoned that if the fertility of $F+ \times F+$ crosses is due to the occurrence of $F-$ cells (?) $F-$ -phenocopy or simply due to temporary loss of F in $F+$ clones, individual $F+ \times F+$ contacts actually being sterile, then treatment of an $F+$ suspension with SM should render it pure $F+$, so that $\underline{A/F+Sm^t \times F+}$ crosses ~~should~~ should behave like $F+ \times F-$ crosses so far as segregation phenomena are concerned.

Here is the result of an experiment.

Cross	No. of prototrophs having phenotype:				Total no. tested
	Lac+Malt+	Lac-Mal-	Lac+Mal-	Lac-Malt+	
$A/F+ \times B/F-$	0	14	1	0	15
$A/F- \times B/F+$	14	0	1	0	15
$A/F+ \times B/F+$	24	24	9	3	60
$\underline{A/F+Sm^t \times B/F+}$	0	22	8	0	30 all culture were
$\underline{A/F+ \times B/F+Sm^t}$	18	0	1	1	20 all culture were

$$A = 58 - 161 = \text{Lac+Malt+} \quad \text{No SM selection or ST tester strains used.}$$

$$B = 19 - 677 = \text{Lac- Mal-} \quad \text{Crosses made on MA + B1.}$$

SM treatment reduced viable counts of both A & B to 5×10^{-5} .

I regard this as valid evidence which, when taken in conjunction with the somewhat similar but less dramatic effect of UV ~~on~~ on either parent in $F+ \times F+$ crosses (about which I wrote you via U.H.), becomes good evidence.

Oh! one other thing. I have been very interested in your $F-$ -phenocopy story but haven't tried to confirm it in aged cultures yet. However I did find that when I mated with washed 24 hr. agar cultures of $58/F+ \times 69/F-$ the prototrophic count was about 100 times less than with young fresh cultures. I thought this might be due to your $F-$ -phenocopy & it turns out to be

No. I crossed a washed 24 hr. agar suspension of S8/F+ with a washed young batch culture of W/F- & of W/F+. The ratios for both crosses were low but that with W/F+ was about twice as great as with W/F-. Testing the markers of prototrophs showed that with W/F+, S8 had behaved almost exclusively as F-, but the ~~crosses~~ prototrophs developing with W/F-, & other markers, showed that S8 still had a good deal of F+ activity. This F-phenotype is a very peculiar business.

Hope you have been able to read my handwriting.

 Bill Hayes
Anne Arbor -